UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,373	09/01/2000	Sean C Semple	INEX.P-007	5857

21121 7590 03/23/2004

OPPEDAHL AND LARSON LLP
P O BOX 5068
DILLON, CO 80435-5068

EXAMINER	
NAFF, DAVID M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,373	SEMPLE ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

The amendment of 12/29/03 amended the specification and claim 1.

Claims examined on the merits are 1-9 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment filed 12/29/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

The new matter results from changing the original disclosure of the specification at paragraph at page 10, lines 21-24 by adding and deleting material . The added material recites "The ionizable lipid is selected such that raising the pH surrounding the small multilamelllar vesicles to a pH of around 7.5 results in the release of external, non-encapsulated oligodeoxynucleotides.

The deleted material recites ", and DOGS".

To provide support the added material to the specification, applicants refer to the specification at page 16, lines 1-2, page 22, lines 17-20 and the examples. However, these portions of the specification set forth neutralizing positive charges of the ionizable amino lipid, DODAP and raising the pH to 7.5 to render the DODAP neutral. This does not support that selecting the ionizable amino lipid was based in raising the pH to around 7.5. The examples and

page 22, lines 17-20 show raising the pH to 7.5 only when using DODAP. The pH of 7.5 is used to release non-encapsulated oligodeoxynucleotides because DODAP selected, and not because DODAP is selected so that raising the pH to around 7.5 releases non-encapsulated oligodeoxynucleotides. Additionally, using pH 7.5 with DODAP does not support using pH 7.5 with any ionizable amino lipid to release non-encapsulated oligodeoxynucleotides, and the disclosure of a pH of 7.5 does not support a pH "around 7.5".

To provide support for deleting DOGS, applicants urge that DOGS is an error, and have provided a 132 Declaration by Michael J. Hope showing that DOGS will have positive charges at pH 7.5 whereas DODAP will have more neutral charges than positive charges at this pH, and that using DOGS at pH 7.5 will not release non-encapsulated oligodeoxynucleotides as is required.

However, the amended specification discloses a pH of "around 7.5" and not a pH of 7.5. At pHs other than 7.5 in the scope of "around 7.5", non-encapsulated oligodeoxynucleotides may be released when using DOGS. Furthermore, the original specification is not limited to pH 7.5, but used pH 7.5 in examples because DODAP is used in the examples. Because DOGS does not work at a pH selected for the use of DODAP does not mean that DOGS will not work at a pH selected to be most suitable for the use of DOGS.

Claim Rejections - 35 USC § 112

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification

in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The original specification fails to support the added limitation to claim 1 reciting "wherein the ionizable lipid is selected such that raising the pH surrounding the small multilamellar vesicles to a pH of around 7.5 results in the release of external, non-encapsulated oligodeoxynucleotides" for reasons set forth above in regard to the same recitation in the specification. The comments set forth above in response to the declaration and arguments also apply to this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing and unclear by "around 7.5" in line 9 of claim 1 being uncertain as to meaning and scope. It would be relative and subjective as to a pH that is around 7.5 and not around 7.5.

In line 6 of claim 1 and line 2 of claim 8, "among" should be replaced with --- the group consisting of --- for a proper Markush group.

Claim Rejections - 35 USC § 103

Claims 1-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheeler et al (WO 96/40964) for reasons set forth in the previous office action of 7/28/03 and for reasons herein.

The claims are drawn to oligodeoxynucleotide-containing lipid vesicles in an aqueous carrier wherein a portion of the vesicles are multilamellar vesicles containing 20-30% ionizable amino lipid, a steric barrier lipid and neutral or sterols, and oligodeoxynucleotides in the lumen or interlamellar spaces of the multilamellar vesicles, wherein the ionizable lipid is selected such that raising the pH surrounding the small multilamellar vesicles to a pH of around 7.5 results in the release of external, non-encapsulated oligodeoxynucleotides from the vesicles.

Wheeler et al disclose encapsulating a therapeutic agent such as antisense oligonucleotides or ribozymes (page 17, lines 14-15) in a lipid bilayer (page 23, lines 3-15, and page 26, line 23) prepared from cationic and non-cationic lipids (page 4, lines 2-7, and page 26, line 17) to provide lipid particles of about 50-150 nm in size containing encapsulated nucleic acid. The cationic lipid is an amino lipid, and cationic lipids that can be used include DOGS (page 15, line 16). The non-cationic lipid may be polyethylene glycol conjugated to ceramides such as PEG-CerC14 (page 25, lines 17-20, and

Table 1 (page 53) and Table 2 (page 54)). As shown in the tables, lipid mixtures containing an amino lipid, a mixture of neutral lipids and a PEG-ceramide are used to encapsulate nucleic acids. The lipid encapsulated nucleic acid can be used to treat a patient by gene therapy to suppress gene expression (paragraph bridging pages 42 and 43).

When the oligonucleotide-containing lipid particles of Wheeler et al contain DOGS as the amino lipid and are multilamellar, the lipid particles are the same as the lipid vesicles of the claims since DOGS is an ionizable amino lipid, and raising the pH to around 7.5 will inherently release some external, non-encapsulated oligodeoxynucleotides.

It would have been obvious to put the oligonucleotide-containing lipid particles of Wheeler et al in an aqueous carrier as claimed for therapeutic use since using an aqueous carrier for a therapeutic agent is well known and conventional.

Response to Arguments

Applicants urge the claims exclude the use of DOGS since DOGS will have positive charges at pH 7.5 as shown by the declaration, and will not work because it will not release external, non-encapsulated oligodeoxynucleotides. However, claim 1 does not require pH 7.5 since the claim recites "around pH 7.5". There is inadequate evidence to support that release of some external, non-encapsulated oligodeoxynucleotides cannot occur at a pH other than 7.5 within the scope of "around 7.5" when the DOGS is the ionizable amino lipid.

Double Patenting

Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-72 of U.S. Patent No. 6,287,591 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently claimed composition would have been obvious from the claims of the patent drawn to a composition and method requiring nucleic acid-containing vesicles where the vesicles can be formed of DSPC, Chol, DODAP and $CerC_{14}$ (claims 19, 37 and 52).

Response to Arguments

Applicants state in the amendment that a terminal disclaimer will be filed when allowable claims are determined.

Allowable Subject Matter

Claims 5 and 9 are free of the prior art.

All claims would be allowable if claims are amended as follows and a terminal disclaimer is submitted to overcome the double patent rejection.

Claim 1,

line 6, cancel "among" and insert --- the group consisting of ---;

line 8, after "ionizable" insert --- amino ---, and after "selected" insert --- from the group consisting of DODAP and DODMA ---, and cancel all of the claim following DODMA from "such" in line 8 to "vesicles" in the last line.

Claim 8, line 2, cancel "among" and insert --- the group consisting of ---.

Conclusion

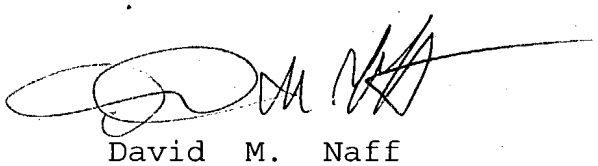
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner
Art Unit 1651

DMN
3/19/04